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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,795	07/02/2002	Thorsten Lehmann-Lintz	5/1269PCT	8945

28505 7590 10/01/2003

BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877

EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/049,795	LEHMANN-LINTZ et al.
Examiner	**Art Unit**
Emily Bernhardt	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *10-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

In accord with 35 USC 121 and 372, applicants are advised that where more than one process of making is claimed along with compounds, the first recited process is considered to form part of the main invention. See 37 CFR 1.475(d). Thus only the first process in claim 18 along with remaining claims is being examined.

Claims 11,12,14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Throughout claim 1 the subject matter appearing after the phrase "wherein the hydrogen atoms are optionally or partially replaced by fluorine atoms" requires clarification. Is the subject matter referring to additional groups that can replace the hydrogen atoms or something else? See R1, R1/R2, Rc and Rd definitions.

2. Other than methylendioxy the definition for fused phenyl rings in the R1/R2 definition is not clear. Heteroaryl, biphenyl are monovalent moieties and thus ortho fusion is not possible.

3. On p.3 first two paragraphs, to what are the groups beginning with "nitro" referring? They cant replace a ring methylene which is what is being recited a few lines above.

4. In the Re definition "from position 2" would better read as "on position 2" .

5. "Containing" in the heteroaryl definitions is open-ended and thus implies more than what is positively recited.

6. Claim 15 is of indeterminate scope as there is no art-recognized disorder known as "lowering plasma levels of atherogenic lipoproteins". Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. Additionally, determining whether a given disease responds or not to a biological mechanism involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two is whether

applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

Claims 10-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. "Isomers" at the end of allthe claims reads on all compounds having the same formula and weight as that depicted in formula (I). Such isomers would certainly have quite different structures and thus different properties from that particularly defined herein. There is no basis by way of any working examples showing such isomers, for having the requisite activity needed to practice the invention. Specification at best describes enantiomers, diastereomers. Insertion of such for "isomers" would not be objected to.

2. Specification provides no adequate support teaching how to use representative scope of instant compounds which can carry an array of heteroaryl groups at every location (except Rb) including fused derivatives at R1/R2. Compounds made (and presumably tested) do not represent such a

scope but rather are closer in structure to each other than to remaining scope as Rc is either alkyl, H or phenyl and Rd is phenyl and Ra is phenyl with substitution thereon represented by R1 choices given on p.2 and R1/R2 fused only with methylenedioxy. However no test data has been presented (or testing protocols) and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree. Thus, there is no reasonable basis for assuming that the myriad of remaining compounds by the generic claims will all share the same physiological properties since they are so structurally dissimilar as to being chemically and biologically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition. Thus given the breadth of the claims, the level of unpredictability in the art and the lack of

direction (i.e. working examples) provided as to what other derivatives might work, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-12 and 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cliffe (US'326) in view of Abou-Gharbia (US'814).

The primary reference teaches very similar compounds to that claimed herein for use as 5-HT1A antagonists. See egs. 26 and 27 which differ in having a methylene vs. instant propylene (i.e. n=3) between piperazine and carbon atom bearing Rc-Re groups. Compounds that are homologs are not considered patentably distinct absent evidence of superior,unexpected results. Note In re Shetty 195 USPQ 753; Ex parte Ruddy 121 USPQ 427;Ex parte Nathan 121 USPQ 349 regarding the patentability of homologs. Also see MPEP 2144.09.

Claims 11 and 12 are also rejected herein since alkyl at instant Rc is also taught by Cliffe. Process of making (route a) is taught in col.5 employing reactants IV and VI.

Abou-Gharbia is applied to show that similar compounds and uses as Cliffe can have methylenes of varying size up to 5 . See main formula in col.1 as well as "n" definition and preferred embodiments in col.2 which include ester derivatives with "n" up to 5 carbon atoms. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to modify the exemplified species of Cliffe by the addition of methylene groups with the expectation that such compounds would also be 5-HT1A antagonists based on the close structural similarity that exists with the prior art compounds (as homologs) and also in view of the equivalency teaching outlined above, and their preparation via instant route a) an obvious expedient in view of the teachings outlined above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by BE'084 (provided by applicants). The patent publication describes a compound within the instant scope as a precursor to an alcohol derivative. See page 3, last two lines of eg.1.

Any inquiry concerning this communication should be directed to Emily Bernhardt at telephone number (703) 308-4714.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

E Bernhardt

EMILY BERNHARDT

PRIMARY EXAMINER

GR UP 1600